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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/701,583	02/05/2001	Karl-Hermann Schlingensiepen	P66141US0	7033

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EXAMINER	
ZARA, JANE J	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 04/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/701,583	SCHLINGENSIEPEN ET AL.	
	Examiner	Art Unit	
	Jane Zara	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 6-11* is/are pending in the application.

4a) Of the above claim(s) *6* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 7-11* is/are rejected.

7)☒ Claim(s) *8* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: _____.

DETAILED ACTION

This Office action is in response to the communication filed 1-31-06.

Claims 1, 2, 6-11 are pending in the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Election/Restrictions

Applicant's additional election of SEQ ID Nos. 9 and 14 in the reply filed on 1-31-06 is acknowledged.

Claim 6 remains withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention as set forth in the prior Office action, there being no allowable generic or linking claim. SEQ ID Nos. 7, 9 and 14, and claims 1, 2, 7-11 have been examined on their merits as set forth below.

Response to Arguments and Amendments

Withdrawn Rejections

Any rejections not repeated in this Office action are hereby withdrawn.

Maintained Objections/Rejections

Claim Objections

Claim 8 is objected to because of the following informalities: in line 5, **"interluekins"** is a misspelling. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2 and 7-9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for the reasons of record set forth in the Office action mailed 4-4-05.

The claims are drawn to a pharmaceutical composition comprising at least one oligonucleotide inhibitor of an immune response selected from SEQ ID Nos. 1-213, and further comprising at least one stimulator positively effecting an immune response, which stimulator enhances the synthesis and/or function of factors selected from GM-CSF, SCF, CSF, IFN, FLT-3-ligand, monocyte chemotactic proteins, IL-2, IL-4, Il-12 and/or IL-18, a virus, viral antigen, tumor or pathogenic antigen, or organ specific antigens expressed in affected organs but not essential for the organism or fusion of dendritic and tumor cells.

Applicant's arguments filed 10-4-05 have been fully considered but they are not persuasive. Applicant argues that adequate written description has been provided for the very broad genus comprising the above mentioned stimulators positively effecting an immune response because the specification dedicates three pages to describe the immuno-stimulating compounds. Applicant argues further that, in order to satisfy the written description requirement, Applicant is not required to embrace in the claims, or describe in the specification, all possible forms in which the claimed principle may be

reduced to practice. Applicants are correct that a laundry list of immuno-stimulating compounds have been provided on pages 3-5 of the instant specification. The recitation of a laundry list of members of this very broad genus, however, does not provide adequate description for the claimed genus which encompasses, but is not limited to a very broad array of molecules and biological agents, including but not limited to *GM-CSF, SCF, CSF, IFN, FLT-3-ligands, monocyte chemotactic proteins, IL-2, IL-4, Il-12 and/or IL-18, any virus or viral antigens, any tumor or pathogenic antigens, and any organ specific antigens expressed in affected organs but not essential for the organism or fusion of dendritic and tumor cells*, which composition provides for treatment effects, as embraced by the claimed term "medicament." Applicants have not provided any treatment effects for a representative number of species of the broad genus claimed, which are used in combination with the negative effector oligonucleotides. the claimed genus embraces a myriad of biological agents as medicaments, none of which are shown in the instant disclosure to provide for the function claimed that of providing treatment effects in an organism. For these reasons, the instant written description rejection is maintained.

Claims 1, 2 and 7-9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the in vitro inhibition of TGF-β expression comprising the administration of antisense oligonucleotides does not reasonably provide enablement for the targeting and inhibition of the TGF-β family in vivo using any antisense or optionally in combination with a tumor cell extract, and which provides for

treatment effects in an organism for the reasons of record set forth in the Office action mailed 4-4-05.

The claims are drawn to therapeutic (pharmaceutical) compositions for treating a neoplasm comprising the administration of a medicament comprising an antisense oligonucleotide of SEQ ID NO: 7, 9, or 14, and further comprising at least one stimulator positively effecting an immune response, which stimulator enhances the synthesis and/or function of factors selected from GM-CSF, SCF, CSF, IFN, FLT-3-ligand, monocyte chemotactic proteins, IL-2, IL-4, Il-12 and/or IL-18, a virus, viral antigen, tumor or pathogenic antigen, or organ specific antigens expressed in affected organs but not essential for the organism or fusion of dendritic and tumor cells.

Applicant's arguments filed 10-4-05 have been fully considered but they are not persuasive. Applicant argues that enablement is satisfied for the entire scope of the presently claimed invention because Fakrai et al (Proc. Natl. Acad. Sci. 93: 2909-2914, 1996) disclose the treatment of tumors in mice following administration of a TGF-beta antisense vector. Contrary to Applicant's assertions, the enablement of Fakrei et al to provide treatment effects in tumor bearing mice by administering a TGF-beta antisense vector does not provide enablement for the instantly claimed invention. The ability of one molecule to provide treatment effects in an animal model does not enable another molecule to do the same, In vivo efficacy is not predictable and it requires undue experimentation beyond that provided in the instant disclosure for the broad array of medicaments claimed. In vitro data provided in the specification is not extrapolatable to in vivo efficacy. The antisense claimed in the instant invention were shown to provide

target gene inhibition in vitro, but not in vivo - alone, or in combination with any member of the very broad genus of immuno-stimulatory compounds claimed. For these reasons, the enablement rejection is maintained.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1, 2, 7, 8, 10 and 11 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 12-15 of copending Application No. 10/984,919. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented. Both sets of claims are drawn to pharmaceutical compositions comprising at least one inhibitor of an immune suppressor (e.g. antisense targeting and inhibiting the expression of TGF-β or its receptors) and one immune stimulator (*see* accompanying sequence alignment data of SEQ ID NOs: 528 and 532 of 10/984,919 and SEQ ID NOs. 7 and 14 respectively of the instant application: They are the same oligonucleotides).

Claims 1, 2, 7, 8, 10 and 11 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1 and 6 of copending Application No. 10/220,033. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented. Both sets of claims are drawn to pharmaceutical compositions comprising at least one inhibitor of an immune suppressor (e.g. antisense targeting and inhibiting the expression of TGF-β or its receptors) and one immune stimulator (*see* accompanying sequence alignment data of SEQ ID NO: 5 of 10/220,033 and SEQ ID NO. 14 of the instant application: They are the same oligonucleotide).

New Rejections

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 7, 8, 10 and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Schlingensiepen et al (WO 94/25588).

Schlingensiepen et al teach pharmaceutical compositions comprising at least one inhibitor of an antisense oligonucleotide of SEQ ID NO: 9, which targets and inhibits the expression of TGF-β or its receptors and one immune stimulator (see the abstract, fig. 8, pages 14, 22, 23, and the accompanying sequence alignment data between SEQ ID NO: 72 of WO 94/25588 and SEQ ID NO: 9 or the instant application).

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 10 and 11 are rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-3 of prior U.S. Patent No. 6,455,689. This is a double patenting rejection.

Schlingensiepen et al (USPN 6,455,689) teach the oligonucleotide of SEQ ID No. 9 for targeting and inhibiting TGF-β (See the accompanying sequence alignment data of SEQ ID NO. 72 of 6,455,689 and SEQ ID NO. 9 of the instant application).

Conclusion

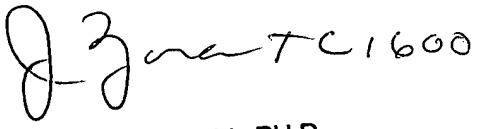
Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. 1.6(d)). The official fax telephone number for the Group is **571-273-8300**. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO

DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(571) 272-0765.** If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, can be reached on (571) 272-0811. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (571) 272-0564. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jane Zara
4-8-06



JANE ZARA, PH.D.
PRIMARY EXAMINER